

**AMENDMENTS TO THE SPECIFICATION**

Please amend the specification as shown:

Please delete the paragraph on page 3, lines 18-29 and replace it with the following paragraph:

The 3-dimensional structure of PBP2x has been determined from a PBP2x containing a deletion of the cytoplasmic and transmembrane regions, referred to as PBP2x\*; this structure has been determined with a resolution of, respectively, 3.5, 2.4, and 3.2 Å, for a  $\beta$ -lactam-sensitive strain of *S. pneumoniae* (strain R6: Pares et al., Nature Struct. Biol., 1996, 3, 284-289; Gordon et al., J. Mol. Biol., 2000, 299, 477-485) and for a resistant clinical isolate (Dessen et al., J. Biol. Chem., 2001, 276, 45106-45112; accession numbers in the database PROTEIN DATA BANK (<http://www.rcsb.org/>), respectively 1PMD, 1QME and 1K25).

Please delete the paragraph on page 5, lines 9-18 and replace it with the following paragraph:

Consequently, a subject of the present invention is a protein derived from a *Streptococcus pneumoniae* PBP2x, characterized in that it consists of a concatenation of the fragments corresponding respectively to the amino acids located between positions 74 to 90, 186 to 199, 218 to 228 and 257-750, with reference to the sequence of the PBP2x protein of the strain R6 (~~SWISSPROT P14677 or GENBANK 18266817~~) **(corresponding to the nucleotide sequence GenBank X16367)**, each one of said fragments being preceded by a peptide fragment of 1 to 7 amino acids.

Please delete the paragraph on page 6, line 7 to page 7, line 3 and replace it with the following paragraph:

For the purpose of the present invention, said *S. pneumoniae* PBP2x protein is defined by the following characteristics:

- it is encoded by the gene referred to as *pbpX*, corresponding to that located in the genome of the *S. pneumoniae* strain R6, between positions 2263 and 4515 of the locus having the NCBI accession number AE008411 or the GENBANK accession number 15457852;

it comprises the following amino acid units (one-letter code), specific to the class B PBPs:

M1: RGXhX(D/S)RSGXXXA	<u>(SEQ ID NO: 10)</u>
M2: (R/K)XXPXG	<u>(SEQ ID NO: 11)</u>
M3: (G/Y)HEXXXDXXL	<u>(SEQ ID NO: 12)</u>
M4: hXX(S/T)hDXXXQ	<u>(SEQ ID NO: 13)</u>
M5: T(G/S)EhhXXXXSPXh(D/N)	<u>(SEQ ID NO: 14)</u>
M6: hEP(A/G)SXXK	<u>(SEQ ID NO: 15)</u>
M7: hXXSXNh	<u>(SEQ ID NO: 16)</u>
M8: K(T/S)G,	

in which the amino acids in bold are strictly conserved in the sequences of class B PBPs; / represents an alternative, for example D/S represents an aspartic acid or a serine; X represents any amino acid; h represents a hydrophobic amino acid and the other letters represent the amino acids most commonly encountered at this position; and

its sequence exhibits, over its entirety, at least 30% identity, preferably at least 50% identity, or at least 85% similarity, with the sequence of the strain R6 (SWISSPROT P14677) (corresponding to the nucleotide sequence GenBank X16367).

Please delete the paragraph on page 8, lines 19-23 and replace it with the following paragraph:

According to another advantageous embodiment of said mini-PBP2x protein, it consists of the concatenation of the fragments, as defined above, of PBP2x of the  $\beta$ -lactam-sensitive *Streptococcus pneumoniae* strain R6 (SWISSPROT P14677) (corresponding to the nucleotide sequence GenBank X16367) and it has the sequence SEQ ID No. 1.

Please delete the paragraph on page 10, lines 3-9 and replace it with the following paragraph:

For instance, if said peptide has 7 amino acids and comprises at position 3 the residue corresponding to position 74 of the mini-PBP2x protein as defined hereabove, therefore, said peptide begins at position 74-2 and ends at position 74+4 in reference to said mini-PBP2x protein and it has the following sequence: Ala-Lys-Arg-Gly-Thr-Ile-Tyr (**SEQ ID NO: 17**).

Please delete the paragraph on page 16, lines 8-15 and replace it with the following paragraph:

-Figure 1 illustrates the amino acid sequence of a mini-PBP2x (SEQ ID No. 1), derived from the PBP2x of the  $\beta$ -lactam-sensitive *S. pneumoniae* strain R6 (**SEQ ID NO: 18**) (**SWISSPROT P14677**) (**corresponding to the nucleotide sequence GenBank X16367**); the amino acids of PBP2x which have been deleted in the mini-PBP2x are replaced with a dash and those of the peptide fragments which have been inserted are represented in italics; the units specific to the class B PBPs are underlined.

Please delete Table 1 and replace it with the following table:

**Table I: Sequence listing**

Identification number	Sequence
SEQ ID No. 1	Mini-PBP2x derived from PBP2x of the strain R6 ( <del>SWISSPROT P14677</del> ) ( <b><u>corresponding to the nucleotide sequence GenBank X16367</u></b> )
SEQ ID No. 2	Primer 5'ICNter
SEQ ID No. 3	Primer 3'ICCter
SEQ ID No. 4	Oligonucleotide mini 1
SEQ ID No. 5	Oligonucleotide mini 2
SEQ ID No. 6	Oligonucleotide mini 3
SEQ ID No. 7	Oligonucleotide mini 4
SEQ ID No. 8	Oligonucleotide mini <i>Ndel</i>

SEQ ID No. 9

Oligonucleotide mini *Xho*I

Please delete the paragraph on page 17, lines 6-13 and replace it with the following paragraph:

A vector for expression of a mini-PBP2x was constructed from the plasmid pGEX-S-PBP2x\*-fl (Mouz et al., J. Biol. Chem., 1999, 274, 19175-19180) containing the sequence encoding the PBP2x\* of the  $\beta$ -lactam-sensitive *S. pneumoniae* strain R6 (fragment 49-750 of the PBP2x of the GENBANK amino acid sequence P14677, corresponding to the GENBANK nucleotide sequence X16367).

Please delete the paragraph on page 19, lines 13-18 and replace it with the following paragraph:

The mini-PBP2x consists of the succession of fragments corresponding respectively to the amino acids located between positions 74 to 93, 184 to 199, 218 to 229 and 257-750 of PBP2x (~~SWISSPROT accession number P14677~~) **(corresponding to the nucleotide sequence GenBank X16367)**, each fragment being preceded, respectively, by the linking fragment GSG, GG, G and GGG.